

08/307621

"=> s transglutaminase"
"L1 107 TRANSGLUTAMINASE"
"=> s collagen"
"L2 8200 COLLAGEN"
"=> s l1 and l2"
"L3 38 L1 AND L2"
"=> d l3 1-38"
" "
"1. 5",514,579," May 7"," 1996"," Human transglutaminases;
Patrick J. O'Hara",""
"et al.", " 435/240.2", " 69.2", " 193", " 254.3", " 320.1;
536/23.2", " 24.31 [IMAGE"
"AVAILABLE] "
" "
"2. 5",510,102," Apr. 23"," 1996"," Plasma and polymer
containing surgical"
"hemostatic adhesives; Kent C. Cochrum", " 424/78.08; 128/DIG.22;
424/530;"
"602/52 [IMAGE AVAILABLE] "
" "
"3. 5",510,077," Apr. 23"," 1996"," Method of making an
intraluminal stent;"
"Thomas Q. Dinh", " et al.", " 264/485", " 279", " 279.1", " 314", "
316", " 320", " 330", " 488"
"[IMAGE AVAILABLE] "
" "
"4. 5",504,001," Apr. 2"," 1996"," Hybrid plasminogen activator;
Donald C."
"Foster", " 435/219; 424/94.64; 435/226 [IMAGE AVAILABLE] "
" "
"5. 5",490,980," Feb. 13"," 1996"," Covalent bonding of active
agents to skin",""
"hair or nails; Norman K. Richardson", " et al.", " 424/94.6; 514/2
[IMAGE"
"AVAILABLE] "
" "
"6. 5",487,889," Jan. 30"," 1996"," Bandage for continuous
application of"
"biologicals; Richard L. Eckert", " et al.", " 424/93.1", " 93.2", "
93.21", " 93.7;"
"514/2", " 12; 604/304", " 305", " 307 [IMAGE AVAILABLE] "
" "
"7. 5",486,599," Jan. 23"," 1996"," Construction and use of
synthetic"
"constructs encoding syndecan; Scott Saunders", " et al.", "
530/395; 435/69.1", "
"69.7", " 252.3", " 320.1; 536/23.4", " 23.5; 935/10", " 47", " 50", "
70 [IMAGE AVAILABLE] "
" "
"8. 5",475,113," Dec. 12"," 1995"," Tetrahydronaphthyl and
thiazole", " oxazole or"
"imidazole substituted ethene derivatives having retinoid-like
activity", "
"reduced skin toxicity and reduced teratogenecity; Roshantha A."

"Chandraratna", " 548/203", " 200", " 204", " 205", " 214", " 235", " 236", " 333.5", " 334.5 [IMAGE"

"AVAILABLE]"

" "

"9. 5", 455, 265, " Oct. 3", " 1995", " Method of treatment with compounds having"

"selective agonist-like activity on RXR retinoid receptors;

Roshantha A."

"S. Chandraratna", " 514/448", " 438", " 444", " 452", " 461", " 467", " 471", " 510", " 531", " 546", ""

569, " 617", " 684", " 700", " 717", " 719", " 729", " 765; 549/60", " 70", " 71", " 72", " 73", " 74", " 75", ""

77, " 78", " 79", " 80", " 369", " 370", " 430", " 448", " 468", " 483", " 486", " 487", " 493", " 495", " 496", ""

497, " 498", " 499", " 501", " 504", " 505", " 506; 560/8", " 100; 562/405", " 490; 564/180; "

"568/327", " 328", " 440", " 592", " 659", " 808; 585/20", " 21 [IMAGE

AVAILABLE]"

" "

"10. 5", 455, 158, " Oct. 3", " 1995", " Fibrin binding domain

polypeptides and uses"

"and methods of producing same; Tikva Vogel", " et al.", " 435/7.21; 424/1.69", ""

"9.341", " 9.4; 435/7.8", " 13; 436/69", " 503", " 504 [IMAGE

AVAILABLE]"

" "

"11. 5", 428, 014, " Jun. 27", " 1995", " **Transglutaminase**

cross-linkable"

"polypeptides and methods relating thereto; Virender Labroo", " et al.", ""

"514/12", " 13", " 14", " 15", " 16; 530/324", " 326", " 327", " 328", " 329", " 345", " 350 [IMAGE"

AVAILABLE]"

" "

"12. 5", 409, 731, " Apr. 25", " 1995", " Method for imparting a

hydrophilic nature"

"to a contact lens; Akira Nakagawa", " et al.", " 427/2.12", " 164", " 338", " 340", " 393.5"

"[IMAGE AVAILABLE]"

" "

"13. 5", 368, 858, " Nov. 29", " 1994", " Methods and compositions

for the treatment"

"and repair of defects or lesions in cartilage; Ernst B.

Hunziker", ""

"424/423", " 424", " 425", " 426", " 450", " 484", " 489", " 499; 514/944", " 953", " 965 [IMAGE"

AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using

fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using

fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using

fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"15. 5",324,840," Jun. 28"," 1994"," Method of treatment with compounds having"
"retinoid-like activity and reduced skin toxicity and lacking teratogenic"
"effects; Roshantha A. S. Chandraratna"," 546/318"," 326"," 335"," 342; 549/77",""
79," 484"," 487"," 496"," 499 [IMAGE AVAILABLE] "
" "
"16. 5",312,751," May 17"," 1994"," Hybridoma producing a monoclonal antibody"
"specific for an antigen of the stratum corneum of human epidermis; Serge"
"Michel"," et al."," 435/240.27"," 70.21"," 172.2; 530/388.2 [IMAGE AVAILABLE] "
" "
"17. 5",271,961," Dec. 21"," 1993"," Method for producing protein microspheres;"
"Edith Mathiowitz"," et al."," 427/213.31; 424/491"," 499; 426/96; 427/213.3",""
"213.36 [IMAGE AVAILABLE] "
" "
"18. 5",270,300," Dec. 14"," 1993"," Methods and compositions for the treatment"
"and repair of defects or lesions in cartilage or bone; Ernst B. Hunziker",""
"514/12; 424/422"," 423"," 424"," 425"," 426"," 450"," 484"," 489"," 499; 514/2"," 8"," 56",""
944," 965; 530/350"," 351"," 353"," 354"," 356"," 840 [IMAGE AVAILABLE] "
" "
"19. 5",270,030," Dec. 14"," 1993"," Fibrin binding domain polypeptide and"
"method of producing; Tikva Vogel"," et al."," 424/1.69"," 9.341"," 9.4; 435/69.1",""
"240.1"," 252.3"," 252.33"," 320.1; 530/350"," 395 [IMAGE AVAILABLE] "
" "
"20. 5",206,023," Apr. 27"," 1993"," Method and compositions for the treatment"
"and repair of defects or lesions in cartilage; Ernst B. Hunziker",""
"424/423"," 422"," 424"," 425"," 426"," 450"," 484"," 489"," 499; 514/2"," 8"," 944"," 953"," 965;"
"530/350"," 351"," 353"," 354"," 356"," 840 [IMAGE AVAILABLE] "
" "
"21. 5",204,447," Apr. 20"," 1993"," Purification of factor XIII; Paul D."
"Bishop"," et al."," 530/381"," 380"," 416"," 417"," 418"," 419"," 420"," 421 [IMAGE AVAILABLE] "
" "
"22. 5",177,092," Jan. 5"," 1993"," Medicinal use of certain tetrazolium salts;"
"David C. Remy"," et al."," 514/381; 548/251 [IMAGE AVAILABLE] "

" "

"23. 5",156,956," Oct. 20"," 1992"," Transgultaminase; Masao Motoki"," et al.", ""
 "435/68.1; 426/573; 435/193 [IMAGE AVAILABLE]"

" "

"24. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in compositions and"
 "methods in thrombolytic therapy; David A. Claremon"," et al.", "
 424/94.64;"
 "514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE
 AVAILABLE]"

" "

"25. 5",151,412," Sep. 29"," 1992"," Pharmaceutically active conjugates having"
 "improved body tissue binding specificity; Robert A. Brown"," 514/8;"
 "435/177; 514/2"," 6"," 21; 530/363"," 380"," 382"," 391.9"," 395"," 400"," 402 [IMAGE"
 "AVAILABLE]"

" "

"26. 5",098,733," Mar. 24"," 1992"," Novel gel-like food articles and process"
 "for producing the same; Nobuo Kyogoku"," et al.", " 426/573"," 104"," 574"," 656;"
 "530/378"," 408 [IMAGE AVAILABLE]"

" "

"27. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; John J. Baldwin"," et al.", "
 424/94.64;"
 "514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE]"

" "

"28. 5",093,028," Mar. 3"," 1992"," Gelled emulsion and process for producing"
 "the same; Nobuo Kyogoku"," et al.", " 252/315.1"," 312; 426/573 [IMAGE"
 "AVAILABLE]"

" "

"29. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; David A. Claremon"," et al.", "
 514/15"," 16"," 18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"30. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; David A. Claremon"," et al.", "
 514/15"," 16"," 18; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"31. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"
 "***transglutaminase** inhibitors; David C. Remy"," et al.", "
 514/384; 546/119;"

"548/251", " 255", " 264.4", " 370.4 [IMAGE AVAILABLE] "

" "

"32. 5",037,664," Aug. 6", " 1991", " Process for producing novel gel-like food"

"articles; Nobuo Kyogoku", " et al.", " 426/573", " 656; 530/408 [IMAGE AVAILABLE] "

" "

"33. 5",030,644," Jul. 9", " 1991", " Imidazole compounds and their use as"

"**transglutaminase** inhibitors; John J. Baldwin", " et al.", " 514/393", " 252", " "

253, " 256", " 278", " 338", " 341", " 395", " 398; 544/333", " 406; 546/15", " 271", " 278; "

"548/302.7", " 307.1", " 321.5", " 324.1 [IMAGE AVAILABLE] "

" "

"34. 5",021,440," Jun. 4", " 1991", " Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David C. Remy", " et al.", " 514/381", " 393", " "

"397; 548/251", " 302.7", " 312.7", " 324.1", " 325.1 [IMAGE AVAILABLE] "

" "

" "

"35. 5",019,572," May 28", " 1991", " Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David A. Claremon", " et al.", " 514/213", " "

"228.2", " 255", " 326", " 398; 540/451; 544/61", " 359; 546/210; 548/302.7", " 314.7", " "

"315.1", " 315.7", " 324.1", " 325.1 [IMAGE AVAILABLE] "

" "

"36. 4",968,713," Nov. 6", " 1990", " Certain imidazole compounds as"

"**transglutaminase** inhibitors; John J. Baldwin", " et al.", " 514/398; "

"548/324.1 [IMAGE AVAILABLE] "

" "

"37. 4",407,787," Oct. 4", " 1983", " Collagenous dressing; Axel Stemberger", " "

"424/444; 106/122", " 125", " 128", " 161; 514/21", " 57", " 801", " 802; 530/356", " 381; "

"602/49", " 50; 604/304 [IMAGE AVAILABLE] "

" "

"38. 4",325,867," Apr. 20", " 1982", " Process for the recovery of"

".alpha.-2-SB-glycoprotein; Walter Eberle", " et al.", " 530/392", " 353", " 354", " 356", " "

381, " 395", " 411", " 413", " 830 [IMAGE AVAILABLE] "

"=> d l3 37 kwic"

" "

"US PAT NO: 4",407,"787 [IMAGE AVAILABLE] L3: 37
of 38"

" "

"ABSTRACT: "

"A collagenous dressing which is characterized in that it contains"
 "**collagen** in combination with a resorbable biopolymer from the group"
 "comprising fibrinogen", "gelatin modified by SH groups", "
 "**collagen**"
 "modified by SH groups", "or regenerated oxycellulose modified by SH groups."
 "Said collagenous dressing is tissue-agglutinable and does not have the"
 "disadvantages of conventional fibrin bonding in combination with"
 "resorbable **collagen**."
 " "
 "SUMMARY: "
 " "
 "BSUM(1) "
 " "
 " **Collagen** has been used in surgery for some time. It can be used in"
 "the form of sponges or fibers to. . . a large area", "the usual"
 "collagenous dressings are inadequate. Attempts have therefore been made"
 "to bond collagenous material", "such as **collagen** or gelatin", "to tissue"
 "by the use of adhesives based on resorcinol-formaldehyde. While such"
 "adhesives are hemostatic", "they are not. . . "
 " "
 "SUMMARY: "
 " "
 "BSUM(2) "
 " "
 " It is known that **collagen** in the body is crosslinked with"
 "constituents of connective tissue. In the process", "
 "**collagen** is"
 "crosslinked through Schiff bases and aldol condensation. It is further"
 "known that in basal membranes tissue strength is enhanced through"
 "disulfide bridges of the basal membrane **collagen**. It is also known to"
 "crosslink proteins such as albumin with intermolecular disulfide bonds"
 "through disulfide bridges after mild reduction. . . network during the"
 "end phase of the plasmatic coagulation. It is also known that individual"
 "fibrin molecules are crosslinked through **transglutaminase**.
 In the"
 "process", "new peptide bonds are formed between glutamic acid and lysine"
 "respectively located on adjacent chains. Through the. . . "

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" The . . . (ie. adhere to) the tissue and which does not have the"

"known drawbacks of fibrin bonding in combination with resorbable"

"**collagen**". Coupled with this object is an improvement to collagenous"

"dressings for local hemostasis."

" "

"SUMMARY: "

" "

"BSUM(4) "

" "

" This object is accomplished through a tissue-adherent collagenous"

"dressing which is characterized in that it contains **collagen** in"

"combination with a resorbable biopolymer from the group comprising"

"fibrinogen", "gelatin modified to contain SH groups", "

collagen modified"

"to contain SH groups", "or oxycellulose modified to contain SH groups."

" "

"SUMMARY: "

" "

"BSUM(5) "

" "

" **Collagen** and fibrinogen or the gelatin modified by SH groups", "

"similarly modified **collagen** or similarly modified oxycellulose may"

"advantageously be combined with each other through freeze drying."

"However", "in the case of a combination of **collagen** and **collagen**"

"modified to contain SH groups it is also possible to introduce SH groups"

"into the **collagen**."

" "

"SUMMARY: "

" "

"BSUM(6) "

" "

" The invention will now be described with reference to a combination of"

"**collagen** and fibrinogen; however", "fibrinogen here takes the place of"

"said resorbable biopolymers", "namely", "gelatin modified to contain SH"

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"=> s lysyl oxidase"
"      1181 LYSYL"
"      5773 OXIDASE"
"L1      51 LYSYL OXIDASE"
"      (LYSYL(W) OXIDASE) "
"=> s transglutaminase"
"L2      107 TRANSGLUTAMINASE"
"=> s l1 and l2"
"L3      1 L1 AND L2"
"=> d l3"
"  "
"1.  5",486,599," Jan. 23"," 1996"," Construction and use of
synthetic"
"constructs encoding syndecan; Scott Saunders"," et al. ","
530/395; 435/69.1",""
"69.7"," 252.3"," 320.1; 536/23.4"," 23.5; 935/10"," 47"," 50","
70 [IMAGE AVAILABLE]"
"=> d l3 kwic"
"  "
"US PAT NO:      5",486,"599 [IMAGE AVAILABLE]                L3: 1
of 1"
"  "
"DETDISC:  "
"  "
"DETD(41) "
"  "
" This . . . the predicted mature protein is located in the
putative"
"transmembrane domain. It also does not appear to be cross-linked
by"
"***lysyl** **oxidase**- or **transglutaminase**-mediated
reactions because"
".beta.-aminopropionitrile and monodansylcadaverine treatments
of NMuMG"
"cells do not change its mobility on SDS-PAGE. Proteins with
regions rich."
"  "
"=> s collagen iii"
"      8200 COLLAGEN"
"      305454 III"
"L4      12 COLLAGEN III"
"      (COLLAGEN(W) III) "
"=> d l4 1-12"
"  "
"1.  5",478,739," Dec. 26"," 1995"," Three-dimensional stromal
cell and tissue"
"culture system; Sandra R. Slivka"," et al. "," 435/240.23","
240.2"," 240.241",""
"240.243; 623/15 [IMAGE AVAILABLE]"
"  "
"2.  5",421,337," Jun. 6"," 1995"," Spectral diagnosis of
diseased tissue;"
"Rebecca Richards-Kortum"," et al. "," 128/665 [IMAGE AVAILABLE]"
"  "

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"3. 5",416,074," May 16"," 1995"," Artificial biological membrane; Michel"
 "Rabaud"," et al.", " 514/21; 530/353", " 356 [IMAGE AVAILABLE] "
 " "

"4. 5",201,745," Apr. 13"," 1993"," Visceral surgery patch; Jean-Louis Tayot", ""
 "et al.", " 606/151; 424/428", " 444; 600/37; 602/50; 623/11", " 66 [IMAGE"
 "AVAILABLE] "
 " "

"5. 5",112,757," May 12"," 1992"," Method for obtaining human hepatocyte"
 "cultures; Christiane Guguen-Guillouzo", " et al.", " 435/240.2", " 240.21 [IMAGE"
 "AVAILABLE] "
 " "

"6. 5",096,593," Mar. 17"," 1992"," Separation material derived from"
 "glucomannan for blood coagulation factor", " preparation and use thereof; "
 "Masaaki Wakita", " et al.", " 210/656", " 198.2", " 502.1; 436/513", " 529; 502/402", ""
 "404; 530/381", " 383", " 413 [IMAGE AVAILABLE] "
 " "

"7. 5",089,422," Feb. 18"," 1992"," Vitro bleeding time determination; Daniel"
 "B. Brubaker", " 436/69; 73/64.41; 422/58", " 73; 436/165", " 809 [IMAGE AVAILABLE] "
 " "

"8. 4",971,964," Nov. 20"," 1990"," Pyridine derivatives; Koji Suzuki", " et al.", ""
 "514/215", " 278", " 290; 540/221", " 543", " 577; 546/17", " 65", " 93 [IMAGE AVAILABLE] "
 " "

"9. 4",939,088," Jul. 3"," 1990"," Sustained production of recombinant gamma"
 "interferon using an Epstein-Barr virus replicon; Janet M. Young", " et al.", ""
 "435/69.51; 424/85.5; 435/240.2", " 240.26", " 320.1 [IMAGE AVAILABLE] "
 " "

"10. 4",897,444," Jan. 30"," 1990"," Immobilized fluorogenic substrates for"
 "enzymes; and processes for their preparation; Paul J. Brynes", " et al.", ""
 "525/54.1; 435/23", " 24; 530/300", " 330", " 331 [IMAGE AVAILABLE] "
 " "

"11. 4",711,783," Dec. 8"," 1987"," Forms of microencapsulation of medicinal"
 "substances by homogeneous layers of native collagen; Alain Huc", " et al.", ""
 "424/460; 106/155", " 161; 424/477", " 491", " 499; 514/773", " 774", " 801; 530/356"
 "[IMAGE AVAILABLE] "

" "

"12. 4",474,761," Oct. 2"," 1984"," Oligopeptides with specific inhibiting"

"properties of collagen induced aggregation"," process for preparing the"

"same and pharmaceutical compositions containing them; Jacques Caen"," et"

"al.," 514/15"," 16"," 822; 530/328; 930/20"," DIG.802 [IMAGE AVAILABLE]"

"=> s 13 and 14"

"L5 0 L3 AND L4"

"=> s 12 and 14"

"L6 0 L2 AND L4"

"=> logoff y"

"U.S. Patent & Trademark Office LOGOFF AT 13:17:33 ON 15 MAY 96"

08/307621

lysyl oxidase ≠

transglutaminase

"=> s transglutaminase or glutaminase"

" 107 TRANSGLUTAMINASE"

" 90 GLUTAMINASE"

"L1 195 TRANSGLUTAMINASE OR GLUTAMINASE"

"=> s scar or mark or bruise"

" 3075 SCAR"

" 70701 MARK"

" 460 BRUISE"

"L2 74010 SCAR OR MARK OR BRUISE"

"=> s l1 and l2"

"L3 14 L1 AND L2"

"=> d l3 1-14"

" "

"1. 5",514,565," May 7"," 1996"," Enzymatically-produced dimeric IL-2 and a"

"nerve-derived **transglutaminase** enzyme for its preparation; Michael"

"Schwartz"," et al.", " 435/68.1 [IMAGE AVAILABLE]"

" "

"2. 5",468,617," Nov. 21"," 1995"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human hepatocellular"

"carcinoma"," and which is a retinoic acid receptor; Hughes Blaudin De The"," "

"et al.", " 435/7.8"," 7.1; 436/63"," 501; 530/350 [IMAGE AVAILABLE]"

" "

"3. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.", " 435/7.21; 424/1.69"," "

"9.341"," 9.4; 435/7.8"," 13; 436/69"," 503"," 504 [IMAGE AVAILABLE]"

" "

"4. 5",378,455," Jan. 3"," 1995"," Cosmetic composition for inhibiting hair"

"growth; George T. E. Kealey"," et al.", " 424/73"," 62"," 70.1"," 70.6"," 401 [IMAGE"

"AVAILABLE]"

" "

"5. 5",376,530," Dec. 27"," 1994"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human hepatocellular"

"carcinoma"," and which is a retinoic acid receptor; Hughes B. De The"," et"

"al.", " 435/6"," 69.1"," 172.3; 530/326"," 327"," 350"," 828; 536/23.1"," 24.31 [IMAGE"

"AVAILABLE]"

" "

"6. 5",317,090," May 31"," 1994"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human

hepatocellular"

"carcinoma", " and which is a retinoic acid receptor; Hughes
Blaudin De The", ""

"et al.", " 530/387.1", " 387.9", " 388.1", " 388.22", " 391.1 [IMAGE
AVAILABLE] "

" "

"7. 5", 270,030, " Dec. 14", " 1993", " Fibrin binding domain
polypeptide and"

"method of producing; Tikva Vogel", " et al.", " 424/1.69", "
9.341", " 9.4; 435/69.1", ""

"240.1", " 252.3", " 252.33", " 320.1; 530/350", " 395 [IMAGE
AVAILABLE] "

" "

"8. 5", 151,412, " Sep. 29", " 1992", " Pharmaceutically active
conjugates having"

"improved body tissue binding specificity; Robert A. Brown", "
514/8; "

"435/177; 514/2", " 6", " 21; 530/363", " 380", " 382", " 391.9", "
395", " 400", " 402 [IMAGE"

"AVAILABLE] "

" "

"9. 4", 762,707, " Aug. 9", " 1988", " New conjugates associating", "
by covalent"

"bond", " an enzyme with an antibody", " and medicinal associations
using the"

"said conjugates; Franz Jansen", " et al.", " 424/180.1", " 94.3
[IMAGE AVAILABLE] "

" "

"10. 4", 701,446, " Oct. 20", " 1987", " Pyrethroid containing
pharmaceutical"

"compositions; Jose A. Arias", " 514/65; 424/711; 514/762", " 895
[IMAGE"

"AVAILABLE] "

" "

"11. 4", 675,313, " Jun. 23", " 1987", " Pyrethroid-containing
pharmaceutical"

"compositions; Jose A. Arias", " 514/65", " 762", " 894", " 934
[IMAGE AVAILABLE] "

" "

"12. 4", 623,626, " Nov. 18", " 1986", " L-glutamic acid oxidase and
its"

"production; Hitoshi Kusakabe", " et al.", " 435/191", " 886 [IMAGE
AVAILABLE] "

" "

"13. 4", 614,714, " Sep. 30", " 1986", " Use of novel L-glutamic
acid oxidase; "

"Hitoshi Kusakabe", " et al.", " 435/25", " 191", " 287.9", " 810", "
817 [IMAGE AVAILABLE] "

" "

"14. 4", 396,628, " Aug. 2", " 1983", " Antiviral activities of
dansylcadaverine"

"and closely related compounds; Ira H. Pastan", " et al.", "
514/603 [IMAGE"

"AVAILABLE] "

"=> d 13 12 kwic"

" "

"US PAT NO: 4",623,"626 [IMAGE AVAILABLE]
of 14"

L3: 12

" "

"SUMMARY: "

" "

"BSUM(22) "

" "

" The . . . screening of glutamic acid producing
microorganisms. Also",""

"since activity assays of enzymes forming glutamic acid as the
product"

"such as **glutaminase**"," glutamic acid-oxaloacetic acid
transaminase"

"(GOT)"," glutamic acid-pyruvic acid transaminase (GPT)"," and"

".gamma.-glutamyl transpeptidase (.gamma.-GTP) can easily be done
by the."

" . . . "

" "

"DETDESC: "

" "

"DETD(38) "

" "

"

94.4"

"NiCl.sub.2"

"

96.5

NaN.sub.3

100.6"

"StCl.sub.2"

"

97.2

DDTC.sup.4

100.7"

"Li.sub.2 SO.sub.4"

"

93.8

Tiron.sup.5

100.7"

"

(trade **mark**)"

"ZnSO.sub.4"

"

90.3"

"

"

".sup.1 EDTA: ethylenediaminetetraacetic acid"

".sup.2 NEM: N--ethylmaleimide"

".sup.3 PCMB: pchloromercuribenzoate"

".sup.4 DDTC: "

"=> s collagen"

"L4 8200 COLLAGEN"

"=> s l1 and l4"

"L5 51 L1 AND L4"

"=> d 15 1-51"

" "

"1. 5",514,579," May 7"," 1996"," Human transglutaminases;
Patrick J. O'Hara",""

"et al.," 435/240.2"," 69.2"," 193"," 254.3"," 320.1;

536/23.2"," 24.31 [IMAGE"

"AVAILABLE]"

" "

"2. 5",510,102," Apr. 23"," 1996"," Plasma and polymer
containing surgical"

"hemostatic adhesives; Kent C. Cochrum"," 424/78.08; 128/DIG.22;

424/530;"
"602/52 [IMAGE AVAILABLE] "
" "
"3. 5",510,077," Apr. 23"," 1996"," Method of making an
intraluminal stent;"
"Thomas Q. Dinh"," et al.," 264/485"," 279"," 279.1"," 314","
316"," 320"," 330"," 488"
"[IMAGE AVAILABLE] "
" "
"4. 5",504,001," Apr. 2"," 1996"," Hybrid plasminogen activator;
Donald C."
"Foster"," 435/219; 424/94.64; 435/226 [IMAGE AVAILABLE] "
" "
"5. 5",490,980," Feb. 13"," 1996"," Covalent bonding of active
agents to skin",""
"hair or nails; Norman K. Richardson"," et al.," 424/94.6; 514/2
[IMAGE"
"AVAILABLE] "
" "
"6. 5",487,889," Jan. 30"," 1996"," Bandage for continuous
application of"
"biologicals; Richard L. Eckert"," et al.," 424/93.1"," 93.2","
93.21"," 93.7;"
"514/2"," 12; 604/304"," 305"," 307 [IMAGE AVAILABLE] "
" "
"7. 5",486,599," Jan. 23"," 1996"," Construction and use of
synthetic"
"constructs encoding syndecan; Scott Saunders"," et al.,"
530/395; 435/69.1",""
"69.7"," 252.3"," 320.1; 536/23.4"," 23.5; 935/10"," 47"," 50","
70 [IMAGE AVAILABLE] "
" "
"8. 5",475,113," Dec. 12"," 1995"," Tetrahydronaphthyl and
thiazole"," oxazole or"
"imidazole substituted ethene derivatives having retinoid-like
activity",""
"reduced skin toxicity and reduced teratogenicity; Roshantha A."
"Chandraratna"," 548/203"," 200"," 204"," 205"," 214"," 235","
236"," 333.5"," 334.5 [IMAGE"
"AVAILABLE] "
" "
"9. 5",455,265," Oct. 3"," 1995"," Method of treatment with
compounds having"
"selective agonist-like activity on RXR retinoid receptors;
Roshantha A."
"S. Chandraratna"," 514/448"," 438"," 444"," 452"," 461"," 467","
471"," 510"," 531"," 546",""
569," 617"," 684"," 700"," 717"," 719"," 729"," 765; 549/60","
70"," 71"," 72"," 73"," 74"," 75",""
77," 78"," 79"," 80"," 369"," 370"," 430"," 448"," 468"," 483","
486"," 487"," 493"," 495"," 496",""
497," 498"," 499"," 501"," 504"," 505"," 506; 560/8"," 100;
562/405"," 490; 564/180;"
"568/327"," 328"," 440"," 592"," 659"," 808; 585/20"," 21 [IMAGE

so A

AVAILABLE] "

" "

"10. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.", " 435/7.21; 424/1.69", ""

"9.341", " 9.4; 435/7.8", " 13; 436/69", " 503", " 504 [IMAGE AVAILABLE] "

" "

"11. 5",428,014," Jun. 27"," 1995"," **Transglutaminase** cross-linkable" ✓

"polypeptides and methods relating thereto; Virender Labroo"," et al.", ""

"514/12", " 13", " 14", " 15", " 16; 530/324", " 326", " 327", " 328", " 329", " 345", " 350 [IMAGE"

"AVAILABLE] "

" "

"12. 5",409,731," Apr. 25"," 1995"," Method for imparting a hydrophilic nature"

"to a contact lens; Akira Nakagawa", " et al.", " 427/2.12", " 164", " 338", " 340", " 393.5"

"[IMAGE AVAILABLE] "

" "

"13. 5",368,858," Nov. 29"," 1994"," Methods and compositions for the treatment" ✓

"and repair of defects or lesions in cartilage; Ernst B. Hunziker", ""

"424/423", " 424", " 425", " 426", " 450", " 484", " 489", " 499; 514/944", " 953", " 965 [IMAGE"

"AVAILABLE] "

" "

"14. 5",366,958," Nov. 22"," 1994"," Localized delivery using fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE] "

" "

"15. 5",352,771," Oct. 4"," 1994"," Hydrolysis of peptide bonds using Pt (II)"

"and Pd (II) complexes; Nenad M. Kostic", " et al.", " 530/345", " 343 [IMAGE"

"AVAILABLE] "

" "

"16. 5",324,840," Jun. 28"," 1994"," Method of treatment with compounds having" } ✓

"retinoid-like activity and reduced skin toxicity and lacking teratogenic"

"effects; Roshantha A. S. Chandraratna", " 546/318", " 326", " 335", " 342; 549/77", ""

79, " 484", " 487", " 496", " 499 [IMAGE AVAILABLE] "

" "

"17. 5",312,751," May 17"," 1994"," Hybridoma producing a monoclonal antibody"

"specific for an antigen of the stratum corneum of human

epidermis; Serge"

"Michel", " et al.", " 435/240.27", " 70.21", " 172.2; 530/388.2
[IMAGE AVAILABLE] "

" "

"18. 5", 292,668, " Mar. 8", " 1994", " Bispecific antibody
determinants; Henry P."

"Paulus", " 436/547; 435/18", " 25", " 240.27; 436/548", " 819;
530/344", " 387.3", " 390.5", ""

"408 [IMAGE AVAILABLE] "

" "

"19. 5", 271,961, " Dec. 21", " 1993", " Method for producing
protein microspheres; "

"Edith Mathiowitz", " et al.", " 427/213.31; 424/491", " 499;
426/96; 427/213.3", ""

"213.36 [IMAGE AVAILABLE] "

" "

"20. 5", 270,300, " Dec. 14", " 1993", " Methods and compositions
for the treatment"

"and repair of defects or lesions in cartilage or bone; Ernst B.
Hunziker", ""

"514/12; 424/422", " 423", " 424", " 425", " 426", " 450", " 484", "
489", " 499; 514/2", " 8", " 56", ""

944, " 965; 530/350", " 351", " 353", " 354", " 356", " 840 [IMAGE
AVAILABLE] "

" "

"21. 5", 270,030, " Dec. 14", " 1993", " Fibrin binding domain
polypeptide and"

"method of producing; Tikva Vogel", " et al.", " 424/1.69", "
9.341", " 9.4; 435/69.1", ""

"240.1", " 252.3", " 252.33", " 320.1; 530/350", " 395 [IMAGE
AVAILABLE] "

" "

"22. 5", 206,023, " Apr. 27", " 1993", " Method and compositions for
the treatment"

"and repair of defects or lesions in cartilage; Ernst B.
Hunziker", ""

"424/423", " 422", " 424", " 425", " 426", " 450", " 484", " 489", " 499;
514/2", " 8", " 944", " 953", " 965; "

"530/350", " 351", " 353", " 354", " 356", " 840 [IMAGE AVAILABLE] "

" "

"23. 5", 204,447, " Apr. 20", " 1993", " Purification of factor
XIII; Paul D."

"Bishop", " et al.", " 530/381", " 380", " 416", " 417", " 418", "
419", " 420", " 421 [IMAGE"

"AVAILABLE] "

" "

"24. 5", 177,092, " Jan. 5", " 1993", " Medicinal use of certain
tetrazolium salts; "

"David C. Remy", " et al.", " 514/381; 548/251 [IMAGE AVAILABLE] "

" "

"25. 5", 158,976, " Oct. 27", " 1992", " Controlling
glutamine/glutamate related"

"neuronal injury; Paul A. Rosenberg", " 514/561 [IMAGE AVAILABLE] "

" "

✓
"26. 5",156,956," Oct. 20"," 1992"," Transgultaminase; Masao Motoki"," et al.", ""
"435/68.1; 426/573; 435/193 [IMAGE AVAILABLE] "
" "
"27. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in compositions and"
"methods in thrombolytic therapy; David A. Claremon"," et al.", ""
424/94.64;"
"514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE AVAILABLE] "
" "
"28. 5",151,412," Sep. 29"," 1992"," Pharmaceutically active conjugates having"
"improved body tissue binding specificity; Robert A. Brown"," 514/8;"
"435/177; 514/2"," 6"," 21; 530/363"," 380"," 382"," 391.9"," 395"," 400"," 402 [IMAGE AVAILABLE] "
" "
"29. 5",135,956," Aug. 4"," 1992"," Method of using cytoprotective alcohols to"
"treat neural disease and neural injury; Jacques Borg"," et al.", "" 514/724"," ""
739," 879 [IMAGE AVAILABLE] "
" "
"30. 5",098,733," Mar. 24"," 1992"," Novel gel-like food articles and process"
"for producing the same; Nobuo Kyogoku"," et al.", "" 426/573"," 104"," 574"," 656;"
"530/378"," 408 [IMAGE AVAILABLE] "
" "
"31. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"
"***transglutaminase** inhibitors; John J. Baldwin"," et al.", "" 424/94.64;"
"514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE] "
" "
"32. 5",093,028," Mar. 3"," 1992"," Gelled emulsion and process for producing"
"the same; Nobuo Kyogoku"," et al.", "" 252/315.1"," 312; 426/573 [IMAGE AVAILABLE] "
" "
"33. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"
"***transglutaminase** inhibitors; David A. Claremon"," et al.", "" 514/15"," 16"," ""
18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE] "
" "
"34. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"
"***transglutaminase** inhibitors; David A. Claremon"," et al.", "" 514/15"," 16"," ""
"18; 530/328"," 329"," 331 [IMAGE AVAILABLE] "

" "

"35. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"
 "***transglutaminase** inhibitors; David C. Remy"," et al.", " 514/384; 546/119;"
 "548/251"," 255"," 264.4"," 370.4 [IMAGE AVAILABLE]"
 " "

"36. 5",037,664," Aug. 6"," 1991"," Process for producing novel gel-like food"
 "articles; Nobuo Kyogoku"," et al.", " 426/573"," 656; 530/408 [IMAGE AVAILABLE]"
 " "

"37. 5",030,644," Jul. 9"," 1991"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; John J. Baldwin"," et al.", " 514/393"," 252"," "
 "253"," 256"," 278"," 338"," 341"," 395"," 398; 544/333"," 406; 546/15"," 271"," 278;"
 "548/302.7"," 307.1"," 321.5"," 324.1 [IMAGE AVAILABLE]"
 " "

"38. 5",021,440," Jun. 4"," 1991"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; David C. Remy"," et al.", " 514/381"," 393"," "
 "397; 548/251"," 302.7"," 312.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"
 " "

"39. 5",019,572," May 28"," 1991"," Imidazole compounds and their use as"
 "***transglutaminase** inhibitors; David A. Claremon"," et al.", " 514/213"," "
 "228.2"," 255"," 326"," 398; 540/451; 544/61"," 359; 546/210; 548/302.7"," 314.7"," "
 "315.1"," 315.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"
 " "

"40. 4",968,713," Nov. 6"," 1990"," Certain imidazole compounds as"
 "***transglutaminase** inhibitors; John J. Baldwin"," et al.", " 514/398;"
 "548/324.1 [IMAGE AVAILABLE]"
 " "

"41. 4",708,861," Nov. 24"," 1987"," Liposome-gel compositions; Mircea C."
 "Popescu"," et al.", " 424/1.21; 264/4.1"," 4.32; 424/1.25"," 450"," 457"," 458"," 460"," "
 "462"," 484; 428/402.2 [IMAGE AVAILABLE]"
 " "

"42. 4",614,714," Sep. 30"," 1986"," Use of novel L-glutamic acid oxidase;"
 "Hitoshi Kusakabe"," et al.", " 435/25"," 191"," 287.9"," 810"," 817 [IMAGE AVAILABLE]"
 " "

"43. 4",532,123," Jul. 30"," 1985"," Dual Microcapsules and process for their"

"preparation; David L. Gardner", " 424/497; 71/DIG.1; 264/4.1", " 4.3; 424/94.3", ""

"DIG.7; 428/402.2", " 402.21 [IMAGE AVAILABLE] "

" "

"44. 4", 472, 498, " Sep. 18", " 1984", " Analysis film and a method of analysis"

"using the same; Nobuhito Masuda", " et al.", " 435/7.7; 422/56", " 57; 435/7.71", ""

"7.72", " 7.9", " 805", " 970; 436/500", " 527", " 537", " 810", " 815 [IMAGE AVAILABLE] "

" "

"45. 4", 444, 878, " Apr. 24", " 1984", " Bispecific antibody determinants; Henry P."

"Paulus", " 435/7.1; 204/403; 422/55; 435/7.5", " 7.91", " 18", " 25", " 28", " 175", " 177", ""

179, " 188", " 287.2", " 287.9", " 805", " 810", " 817", " 962", " 964", " 966", " 969; 436/512", " 518", ""

528, " 530", " 548", " 808 [IMAGE AVAILABLE] "

" "

"46. 4", 407, 787, " Oct. 4", " 1983", " Collagenous dressing; Axel Stemberger", ""

"424/444; 106/122", " 125", " 128", " 161; 514/21", " 57", " 801", " 802; 530/356", " 381; "

"602/49", " 50; 604/304 [IMAGE AVAILABLE] "

" "

"47. 4", 325, 867, " Apr. 20", " 1982", " Process for the recovery of"

".alpha.-2-SB-glycoprotein; Walter Eberle", " et al.", " 530/392", " 353", " 354", " 356", ""

381, " 395", " 411", " 413", " 830 [IMAGE AVAILABLE] "

" "

"48. 4", 307, 195, " Dec. 22", " 1981", " Immobilized enzyme membrane; Yoshiharu"

"Karasawa", " et al.", " 435/287.9; 204/403; 435/179", " 181", " 182 [IMAGE AVAILABLE] "

" "

"49. 4", 061, 141, " Dec. 6", " 1977", " Apparatus and method for selectively"

"separating amino acids and defined proteins in blood; Viktor Holger"

"Hyden", " et al.", " 604/5; 128/DIG.3; 422/44; 435/14", " 177", " 179", " 181", " 182", ""

"293.1", " 297.2", " 299.1 [IMAGE AVAILABLE] "

" "

"50. 3", 849, 254, " Nov. 19", " 1974", " PROCESS FOR EFFECTING ENZYMATIC REACTIONS"

"IN AEROSOLS; Donald J. Kirwan", " et al.", " 435/176", " 179", " 180", " 199", " 213", " 236", ""

822, " 882", " 885 [IMAGE AVAILABLE] "

" "

"51. 3", 839, 175, " Oct. 1", " 1974", " ELECTRODEPOSITION OF ENZYMES; Melvin H."

"Keyes", " 435/176; 204/489; 435/283.1", " 287.9", " 817 [IMAGE AVAILABLE] "

"=> d 15 26 kwic"

" "

"US PAT NO: 5",156,"956 [IMAGE AVAILABLE]
of 51"

L5: 26

" "

"ABSTRACT: "

"A **transglutaminase** catalyzing an acyl transfer reaction of
a"

".gamma.-carboxyamide group of a glutamine residue in a peptide
or protein"

"chain in. . . "

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" The present invention relates to a novel **transglutaminase**
and a"

"process for producing a protein gelation product using the"

"**transglutaminase**."

" "

"SUMMARY: "

" "

"BSUM(9) "

" "

" Up to now", " however", " no report has been made on any
transglutaminase"

"derived from microorganisms. With respect to a process for
producing gel"

"products of protein using an animal-derived

"**transglutaminase**", " the"

"present inventors have already made investigations resulting in
Published"

"Unexamined Japanese Patent Application No. 149645/83."

" "

"SUMMARY: "

" "

"BSUM(10) "

" "

" However", " application of the animal-derived

"**transglutaminase** to"

"industry", " particularly", " the process for producing protein
gelation"

"products involves defects as described below."

" "

"SUMMARY: "

" "

"BSUM(11) "

" "

" It . . . substrate protein and at least 2.0 wt. % of a
substrate"

"protein concentration are required for gelation. Further", " the"

"animal-derived **transglutaminase** is calcium

(Ca.sup.2+) dependent so"

"that its application is limited."

" "

"DRAWING DESC: "

" "

"DRWD(8) "

" "

" Accordingly", " an object of the present invention is to provide a new"

"**transglutaminase** which is free from problems such as quantity of"

"supply", " cost/performance", " and ease of purification."

" "

"DRAWING DESC: "

" "

"DRWD(9) "

" "

" It is another object of the present invention to provide a"

"**transglutaminase** which has great practicality since no calcium is"

"required for the reaction catalyzed by the

"**transglutaminase**."

" "

"DRAWING DESC: "

" "

"DRWD(10) "

" "

" The present invention is further directed to a method for producing a"

"protein gelation product by using a **transglutaminase**."

" "

"DRAWING DESC: "

" "

"DRWD(11) "

" "

" The above and other objects which will become more readily apparent"

"hereinafter", " have been achieved by the discovery of a novel"

"**transglutaminase** derived from microorganisms."

" "

"DRAWING DESC: "

" "

"DRWD(13) "

" "

" Animal-derived . . . been investigated heretofore but due to lack of"

"practicability", " the present inventors have made wide-ranging"

"investigations", " searching for a microorganism-derived"

"**transglutaminase**. As a result", " it has been found that bacteria"

"belonging to the genus Streptoverticillium are capable of producing novel"

"transglutaminases. . . . "

" "

"DRAWING DESC: "

" "

"DRWD(15) "

" "

" Methods for culture", " purification", " etc.", " which comprise culturing these"

"microorganisms and harvesting **transglutaminase** (hereafter referred to"

"as BTGase) will be described below. For the purposes of the present"

"invention", " any culturing mode of. . . "

" "

"DRAWING DESC: "

" "

"DRWD(28) "

" "

" Enzymological properties of the thus obtained purified BTGases", " namely", "

"**transglutaminase** of Streptoverticillium mobaraense IFO 13819 (named"

"BTG-1)", " **transglutaminase** of Streptoverticillium griseocarneum IFO"

"12776 (named BTG-2) and **transglutaminase** of Streptoverticillium"

"cinnamoneum sub sp. cinnamoneum IFO 12852 (named BTG-3) are described"

"below."

" "

"DRAWING DESC: "

" "

"DRWD(51) "

" "

" Next", " properties of BTGases are compared to those of guinea pig"

"liver-derived **transglutaminase**. The guinea pig liver-derived"

"**transglutaminase** was prepared by the method described in Published"

"Unexamined Japanese Patent Application No. 149645/83. In Table 4", "

"comparison in enzymological. . . in Table 5. As will be apparent from"

"Tables 4 and 5", " various differences in enzymological properties are noted"

"between **transglutaminase** of guinea pig liver (hereafter referred to"

"as MTGase) which has been mainly investigated heretofore and BTGases"

"derived from actinomycetes;. . . "

" "

"DRAWING DESC: "

" "

"DRWD(55) "

" "

" First", " . . . therefrom. The kind of animal protein is not"

"particularly limited but there may be mentioned", " for example", " milk"
 "protein", " gelatin", " **collagen**", " serum albumin", " etc."
 " "
 "DETD(4) "
 " "
 " The . . . by Rohm & Haas Co.", " Ltd.)", " which had been previously"
 "equilibrated with 0.05M phosphate buffer (pH 6.5). By this operation", ""
 "**transglutaminase** was adsorbed. After washing protein impurities out"
 "with the buffer", " a density gradient of 0.05 to 0.5M was prepared by. . ."
 ". have a conductivity of 10 ms or less", " it was passed through a column"
 "of blue Sepharose. By this operation", " **transglutaminase** was adsorbed."
 "After washing protein impurities out with 0.05M phosphate buffer (pH 7)", ""
 "a density gradient of 0 to 1M. . . . "
 " "
 "DETD(63) "
 " "
 " A necessary amount of oxhide-derived atelo-**collagen** powders"
 "(manufactured by Kouken K.K.) were taken in a test tube and 2 ml of 0.1M"
 "Tris-HCl buffer (pH 7.5). . . maintaining in a water bath at"
 "55.degree. C. for 15 minutes", " the mixture was stirred to prepare 3 to 10%"
 "atelo-**collagen** solutions. Before the solutions of high concentration"
 "were gelled due to cooling", " BTGase was added thereto in 0.05 U/mg protein"
 "followed by incubation at 55.degree. C. for 60 minutes. As a control for"
 "the all samples", " 10% atelo-**collagen** solution with no BTGase added was"
 "also incubated likewise. Immediately after completion of the incubation", ""
 "the system was allowed to. . . . "
 " "
 "CLAIMS: "
 " "
 "CLMS(1) "
 " "
 " What is claimed as new and desired to be secured by Letters Patent of"
 "the United States:"

" "

" 1. A ****transglutaminase**** which catalyzes an acyl transfer reaction of a"

".gamma.-carboxyamide group of a glutamine residue in a peptide or protein"

"chain. . . "

" "

"CLAIMS: "

" "

"CLMS(2) "

" "

" 2. The ****transglutaminase**** of claim 1"," obtained from a microorganism of"

"the genus Streptovercillium."

" "

"CLAIMS: "

" "

"CLMS(3) "

" "

" 3. A process for producing a ****transglutaminase****"," which comprises"

"culturing a microorganism of a strain belonging to the genus"

"Streptovercillium capable of producing a ****transglutaminase**** which"

"catalyzes an acyl transfer reaction of a .gamma.-carboxyamide group of a"

"glutamine residue in a peptide or protein chain independently of"

"Ca.sup.2+"," and harvesting said ****transglutaminase**** from the culture."

" "

"CLAIMS: "

" "

"CLMS(4) "

" "

" 4. . . . which comprises contacting a protein-containing solution or"

"slurry having a protein concentration of at least 1.0 wt. % with a"

"****transglutaminase**** which catalyzes an acyl transfer reaction of a"

".gamma.-carboxyamide group of a glutamine residue in a peptide or protein"

"chain. . . "

" "

"CLAIMS: "

" "

"CLMS(5) "

" "

" 5. A process as claimed in claim 4 wherein 0.01 to 2000 units of said"

"****transglutaminase**** are incorporated per 1.0 g of the protein contained"

"in said solution or slurry."

" "

"CLAIMS: "

" "

"CLMS(6) "

" "

" 6. The process of claim 4", " wherein said **transglutaminase** is obtained"

"from the genus Streptoverticillium."

"=> d 15 37 kwic"

" "

"US PAT NO: 5",030,"644 [IMAGE AVAILABLE]
of 51"

L5: 37

"TITLE: Imidazole compounds and their use as

transglutaminase"

" inhibitors"

" "

"ABSTRACT: "

"Imidazole compounds including imidazoles and imidazolium salts", " and their"

"use as **transglutaminase** inhibitors are disclosed."

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" A number of disease states have been associated with"
transglutaminase activity Thus", " for example", " in acne lesions", ""

transglutaminase activity in sebaceous follicles has been reported by"

"DeYoung et. al.", " in J. Investigative Dermatology", " 82", " 275 (1984). Also", ""

"the cornified cell envelope in acne has been reported to be a result of"

transglutaminase activity by Dalziel et. al.", " Br. J. Exp. Pathology", ""

" "

"SUMMARY: "

" "

"BSUM(4) "

" "

" Another dermatological disease", " psoriasis", " is reported to be associated"

"with excessive **transglutaminase** activity by Bernard et. al. British"

"Journal of Dermatology", " 114", " 279 (1986)"

" "

"SUMMARY: "

" "

"BSUM(5) "

" "

" Cataracts also have been reported to be associated with elevated"

transglutaminase activities."

" "

"SUMMARY: "

" "

"BSUM(6) "

" "

" Factor XIIIa is a plasma **transglutaminase** which is the activated"

"form of Factor XIII also known as fibrinase or fibrin stabilizing factor."

"It is essential for. . . "

" "

"SUMMARY: "

" "

"BSUM(11) "

" "

" A novel class of imidazole compounds has been discovered which inhibits"

"**transglutaminase** activity", " particularly Factor XIIIa activity. The"

"invention also embraces composition and methods for using the imidazole"

"compounds as Factor XIIIa. . . . "

" "

"DETDESC: "

" "

"DETD(43) "

" "

" The compounds of the present invention are useful as"

"**transglutaminase** inhibitors", " particularly as Factor XIIIa inhibitors", ""

"and are adapted to be employed in thrombolytic therapy. In such use", " it"

"is. . . . "

" "

"DETDESC: "

" "

"DETD(45) "

" "

" Also", " . . . frequently Arg-Gly-Asp. Some classes of natural proteins"

"having this property are fibrinogen receptor antagonists", " thromboxane"

"receptor antagonists", " thromboxane synthesis inhibitors", " **collagen**"

"receptor antagonists and thrombin inhibitors. Among especially useful"

"polypeptides are those designated Echistatin and Bitistatin and" "having the amino acid. . . . "

" "

"DETDESC: "

" "

"DETD(47) "

" "

" The preferred compounds for use as **transglutaminase**"

inhibitors are"
"the quaternary imidazolium salts."

" "
"DETDESC: "
" "

"DETD(83) "
" "

" The preparation of the imidazole compounds suitable for
inhibiting"
"***transglutaminase** enzymes", " particularly Factor XIIIa", " and
compositions"

"suitable for carrying out the process of the present invention
are"

"illustrated by the. . . "

"=> s amine or amino"

" 120602 AMINE"

" 128100 AMINO"

" "

L6 182505 AMINE OR AMINO"

"=> s 15 and 16"

"L7 47 L5 AND L6"

"=> s spermidine or putrescine"

" 776 SPERMIDINE"

" 351 PUTRESCINE"

"L8 999 SPERMIDINE OR PUTRESCINE"

"=> s 17 and 18"

"L9 20 L7 AND L8"

"=> d 19 1-20"

" "

"1. 5",490,980," Feb. 13", " 1996", " Covalent bonding of active
agents to skin", ""

"hair or nails; Norman K. Richardson", " et al.", " 424/94.6; 514/2
[IMAGE"

"AVAILABLE] "

" "

"2. 5",475,113," Dec. 12", " 1995", " Tetrahydronaphthyl and
thiazole", " oxazole or"

"imidazole substituted ethene derivatives having retinoid-like
activity", ""

"reduced skin toxicity and reduced teratogenecity; Roshantha A."

"Chandraratna", " 548/203", " 200", " 204", " 205", " 214", " 235", "

236", " 333.5", " 334.5 [IMAGE"

"AVAILABLE] "

" "

"3. 5",455,265," Oct. 3", " 1995", " Method of treatment with
compounds having"

"selective agonist-like activity on RXR retinoid receptors;
Roshantha A."

"S. Chandraratna", " 514/448", " 438", " 444", " 452", " 461", " 467", "
471", " 510", " 531", " 546", ""

569, " 617", " 684", " 700", " 717", " 719", " 729", " 765; 549/60", "

70", " 71", " 72", " 73", " 74", " 75", ""

77, " 78", " 79", " 80", " 369", " 370", " 430", " 448", " 468", " 483", "

486", " 487", " 493", " 495", " 496", ""

497," 498"," 499"," 501"," 504"," 505"," 506; 560/8"," 100;
562/405"," 490; 564/180;"
"568/327"," 328"," 440"," 592"," 659"," 808; 585/20"," 21 [IMAGE
AVAILABLE]"

" "

"4. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain
polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.,"
435/7.21; 424/1.69"," "

"9.341"," 9.4; 435/7.8"," 13; 436/69"," 503"," 504 [IMAGE
AVAILABLE]"

" "

"5. 5",366,958," Nov. 22"," 1994"," Localized delivery using
fibronectin"

"conjugates; Alan L. Weiner"," et al.," 514/2; 424/450;
530/380"," 810"," 812"

"[IMAGE AVAILABLE]"

" "

"6. 5",324,840," Jun. 28"," 1994"," Method of treatment with
compounds having"

"retinoid-like activity and reduced skin toxicity and lacking
teratogenic"

"effects; Roshantha A. S. Chandraratna"," 546/318"," 326","
335"," 342; 549/77"," "

79," 484"," 487"," 496"," 499 [IMAGE AVAILABLE]"

" "

"7. 5",270,030," Dec. 14"," 1993"," Fibrin binding domain
polypeptide and"

"method of producing; Tikva Vogel"," et al.," 424/1.69","
9.341"," 9.4; 435/69.1"," "

"240.1"," 252.3"," 252.33"," 320.1; 530/350"," 395 [IMAGE
AVAILABLE]"

" "

"8. 5",204,447," Apr. 20"," 1993"," Purification of factor XIII;
Paul D."

"Bishop"," et al.," 530/381"," 380"," 416"," 417"," 418","
419"," 420"," 421 [IMAGE

"AVAILABLE]"

" "

"9. 5",177,092," Jan. 5"," 1993"," Medicinal use of certain
tetrazolium salts;"

"David C. Remy"," et al.," 514/381; 548/251 [IMAGE AVAILABLE]"

" "

"10. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in
compositions and"

"methods in thrombolytic therapy; David A. Claremon"," et al.,"
424/94.64;"

"514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE
AVAILABLE]"

" "

"11. 5",135,956," Aug. 4"," 1992"," Method of using
cytoprotective alcohols to"

"treat neural disease and neural injury; Jacques Borg"," et
al.," 514/724"," "

739," 879 [IMAGE AVAILABLE]"

" "

"12. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; John J. Baldwin"," et al.",," 424/94.64;"

"514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE]"

" "

"13. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David A. Claremon"," et al.",," 514/15"," 16"," "

18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"14. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David A. Claremon"," et al.",," 514/15"," 16"," "

"18; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"15. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"

"**transglutaminase** inhibitors; David C. Remy"," et al.",," 514/384; 546/119;"

"548/251"," 255"," 264.4"," 370.4 [IMAGE AVAILABLE]"

" "

"16. 5",030,644," Jul. 9"," 1991"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; John J. Baldwin"," et al.",," 514/393"," 252"," "

253," 256"," 278"," 338"," 341"," 395"," 398; 544/333"," 406; 546/15"," 271"," 278;"

"548/302.7"," 307.1"," 321.5"," 324.1 [IMAGE AVAILABLE]"

" "

"17. 5",021,440," Jun. 4"," 1991"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David C. Remy"," et al.",," 514/381"," 393"," "

"397; 548/251"," 302.7"," 312.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"

" "

"18. 5",019,572," May 28"," 1991"," Imidazole compounds and their use as"

"**transglutaminase** inhibitors; David A. Claremon"," et al.",," 514/213"," "

"228.2"," 255"," 326"," 398; 540/451; 544/61"," 359; 546/210; 548/302.7"," 314.7"," "

"315.1"," 315.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"

" "

"19. 4",968,713," Nov. 6"," 1990"," Certain imidazole compounds as"

"**transglutaminase** inhibitors; John J. Baldwin"," et al.",," 514/398;"

"548/324.1 [IMAGE AVAILABLE]"